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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/663,889	09/18/2000	Gary J. Nabel	8642/91	6450

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

MC

Office Action Summary	Application No.	Applicant(s)	
	09/663,889	NABEL ET AL.	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17 and 19-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17 and 19-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and argument of 6/9/05 are entered.

Claims 21 and 35-36 are amended.

Claims 17 and 19-36 are presently pending and considered.

Appeal Meeting and Decision

On April 6, 2005 a meeting was held between Examiner Kelly and Supervisory Patent Examiners Ram Shukla and Amy Nelson. It is noted that Ram Shukla was the Examiner's Primary Examiner on the previous Official Actions, and that Amy Nelson was a SPE outside of the Examiner's Art Unit at the time of the meeting. At the meeting, it was decided that the Examiner would withdraw finality and issue the following Action in order to make the Examiner's arguments more clear for the Appeal process.

Accordingly, Finality is withdrawn with this Action.

Priority

Applicant's claim of priority to U.S. Serial Nos. 08/533,942, 09/031,572, and 09/426,325, filed 9/26/95, 2/26/98, and 10/25/99, respectively, remain denied for reasons of record in the Official Action of 29 January 2004, pp. 2-4 and the Official Action of 8/26/04, pp. 2-4.

The rejection is maintained because Applicant's disclosure is drawn to a **combination** which comprising a nucleic acid comprising a generic gene encoding p21 and a generic catheter.

Specifically, Applicant's priority is denied for the claimed combinations because prior to the present Application, no such combination was claimed, and Applicant relies on the implicit

disclosure common to the various Applications wherein a double-balloon catheter was used to deliver adenoviral vectors comprising a p21-encoding sequence operably linked to expression control elements, into the iliofemoral artieries of Yorkshire pigs (e.g., SPECIFICATION, p. 14, paragraphs 2-3).

Such double-balloon catheter, used as a vehicle to inject the vector, does satisfy the written description requirements for the breadth of the claimed combinations to demonstrate that Applicant possessed a generic combination comprising a generic catheter and a generic p21 gene, as a product. Further to emphasize the point that Applicant has not, prior to the present Application demonstrated possession of such a generic combination, Applicant's specifications, including the present specification, do not discuss the importance of medical delivery devices whatsoever, but simply use one such device, the double balloon catheter in Applicant's administration of adenoviral vectors. As such, Applicant must be relying on obviousness to support the breadth of the vectors and devices claimed.

Repeated support has been sought in the decisions of *Univ. of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ.2d 1398, 1405 and *Lockwood v. American Airlines, Inc.* (Fed. Cir. 1997) 41 USPQ.2d 1961, 1966. In these decisions, it has been repeatedly held that a description which renders obvious a claimed invention does not satisfy the written description requirement of that invention. Applicant is reminded that material needed to accord an application a filing date may not be incorporated by reference. Therefore, if a continuation or divisional application as originally-filed incorporates by reference material omitted from the application papers, which is needed to accord the application a filing date, the application will not be entitled to a filing date. MPEP 201.06(c).

Accordingly, priority to the parent applications remains denied, except for that particular genera of a double-balloon catheter and the viruses used in EXAMPLE 1.

Response to Arguments - Priority

Applicant's arguments of 6/9/05 have been fully considered but are not found persuasive.

Applicant argues that the disclosure of Applicant's specifications (reviewed above) specifically describe the combination of a catheter and a nucleic acid encoding p21, and therefore, support is not found through obviousness, but is found by express description of the subject matter (Applicant's argument of 6/9/05, p. 11, paragraph 2).

Such is not persuasive. Applicant's specific disclosure is for the use of a double-balloon catheter as a vehicle to transfer an adenoviral vector into porcine iliofemoral arteries (ABOVE; EXAMPLE 1 of each specification). Such disclosure does not amount to meeting the written description requirement, but simply that Applicant contemplated using a double-balloon catheter to deliver a specific adenovirus encoding p21 into pig iliofemoral arteries. As stated in, e.g., *Lockwood* at 1966, "One shows that one is 'in possession' of the invention by describing the invention, with all its claimed limitations, not that which makes it obvious." Applicant, through the use of a single catheter to inject such p21, encoded in a single adenoviral species, into porcine iliofemoral arteries, necessarily relies on obviousness. Necessarily, the other forms of catheters and carriers are therefore argued to be possessed by obviousness type satisfaction.

Applicant argues that the use of *Lilly* as a citation of case law in not appropriate. The argument is that Lilly did not describe a particular biological sequence, and Applicant has described the combination of a catheter and nucleic acid encoding p21. Therefore, Applicant

argues, such case law is not applicable in its reasoning. (Applicant's argument of 6/9/05, p. 11, paragraph 3.)

Such is not persuasive. First, as noted in the previous argument, Applicant has described but one thing (equivalent to a sequence of Lilly): the balloon catheter and p-21 encoding adenoviral vectors, for delivery of a gene to porcine iliofemoral artery. Applicant has not disclosed the structure of other forms of catheter, e.g., single-balloon, triple-balloon, non-balloon catheters, and hence, Lilly does agree that no support is present for these combinations. Also, for the core of the invention, the double-balloon catheter and adenovirus encoding p21, Lilly cites to Lockwood, which Applicant does not deny provides appropriate support for the Examiner's argument. Hence, both Lilly and Lockwood support the Examiner's argument.

Oath/Declaration

The requirement for a new oath/declaration is maintained for reasons of record, e.g., the Official Action of 8/26/04, p. 4, paragraph 5 and the Official Action of 1/29/04, pp. 4-5, paragraph bridging.

Response to Arguments – Oath/Declaration

Applicant's arguments of 6/9/05 have been fully considered but are not found persuasive.

Applicant avers that, similar to the present specification, the previously-filed specifications, which disclose the same method of injecting adenoviral vectors, support that presently claimed combination, and therefore, Applicant's new oath is unnecessary (Applicant's argument of 6/9/05, pp. 11-12, paragraph bridging).

Such is not persuasive. As has been demonstrated above, with respect to priority, Applicant's claimed subject matter is deemed not to provide adequate written description, and therefore priority is denied and a new is required.

Claim Rejections – 35 USC 112, first paragraph – new matter

Claims 17 and 19-36 remain rejected for reasons of record, for failing to comply with the written description requirement (Official Action of 29 January 2004, pp. 5-7; Official Action of 8/26/04, pp. 5-6).

For similar reasons as provided for the denial of priority, it is argued that Applicant does not have adequate written description, and hence are new matter, for a generic combination comprising a generic catheter and a generic p21-encoding gene.

Specifically, the claimed combinations lack written description because Applicant relies on the implicit disclosure common to the various Applications wherein a double-balloon catheter was used to deliver adenoviral vectors comprising a p21-encoding sequence operably linked to expression control elements, into the iliofemoral artieries of Yorkshire pigs (e.g., SPECIFICATION, p. 14, paragraphs 2-3).

Such double-balloon catheter, used as a vehicle to inject the vector, does satisfy the written description requirements for the breadth of the claimed combinations to demonstrate that Applicant possessed a generic combination comprising a generic catheter and a generic p21

gene, as a product. Further to emphasize the point that Applicant has not, prior to the present Application demonstrated possession of such a generic combination, Applicant's specifications, including the present specification, do not discuss the importance of medical delivery devices whatsoever, but simply use one such device, the double balloon catheter in Applicant's administration of adenoviral vectors. As such, Applicant must be relying on obviousness to support the breadth of the vectors and devices claimed.

Repeated support has been sought in the decisions of *Univ. of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ.2d 1398, 1405 and *Lockwood v. American Airlines, Inc.* (Fed. Cir. 1997) 41 USPQ.2d 1961, 1966. In these decisions, it has been repeatedly held that a description which renders obvious a claimed invention does not satisfy the written description requirement of that invention.

Response to Arguments – new matter

Applicant's arguments of 6/9/05 have been fully considered but are not found persuasive.

Applicant argues that the term "combination" would naturally occur to the Artisan to describe the presently-claimed invention (Applicant's argument of 6/9/05, p. 6, paragraph 1).

Such is persuasive, and as such, the term "combination" itself is not rejected for being new matter; however, the generic combinations presently claimed lack written description for the reasons given above, i.e., Applicant is necessarily relying on obviousness to satisfy the written description requirement (see above).

Applicant argues that the invention was reduced to actual practice in the subject specification, as well as the parent specifications to this Application, and that it clearly conveys to the Artisan that a generic combination comprising a generic catheter and generic p21 gene are

possessed by the Applicant at the time of invention (Applicant's argument of 6/9/05, p. 6, paragraph 1).

Such is not persuasive. The Examiner does not deny that Applicant has possession of the specific double-balloon catheter and adenoviral vector comprising a p21 gene, but that the broad genera claimed rely on obviousness to satisfy written description (above).

Applicant argues, through analogy to *In re Smythe and Shamos*, that the art is not unpredictable, and therefore, Applicant's specification necessarily provides adequate written description for the broad generic combinations claimed. (Applicant's argument of 6/9/05, p. 6, paragraph 2.)

Such is not persuasive. In *Smythe*, a non-biological machine is described, and the requirements for the disputed limitations are fully described (i.e., inert fluid), and the Examiner agrees that in such a case, the specific properties are given such that the artisan would necessarily understand that *Smythe* had possession of such inert fluids, whether gas or liquid. Applicant, however, does not demonstrate that the instant specification describes the requirements of the generic combination are fully described such that the Artisan would understand that Applicant had possession of the invention. Instead, in the instant case, Applicant relies on implicit support where a specific double-balloon catheter was used, without any description of how to administer any generic p21 gene to any site using any generic catheter. Applicant's description is lacking even in description as to whether the specific adenoviral vectors comprising the p21 gene were administered as a coating on the balloon(s) of the catheter or in the inter-balloon space. Hence, the Artisan would not understand Applicant to have possessed any generic combination of any generic catheter and any gene encoding p21. To wit,

catheters may also be single-balloon catheters, triple balloon or even more balloon catheters, or even not have a balloon. If Applicant delivered the vector through the inter-balloon space, how would a single balloon or a no-balloon catheter deliver such substance? If Applicant delivered it in the inter-balloon space, which interballoon space would be the space into which any particular vector should be delivered? Does the type of vector influence balloon choice? Simply put, Applicant's reliance on implicit disclosure demonstrates that Applicant does not possess the broadly claimed genera, or even contemplated it. Applicant has not even discussed choice of medical device.

Applicant argues through the dicta in *In re Smythe*, that the art is predictable and therefore provides adequate written description (Id.).

Such is not persuasive. The cited passage indicates that if a lead weight was used in weighing an item in a specification, the claims may indicate any metal or any weight of the same weight, and analogizes that the specification, as in *In re Smythe* describes the requirements for performing the function, and therefore, written description is met. In the instant case, however, as demonstrated in the last answer, Applicant has failed to address the breadth claimed. This is not a case, like that of mechanical and electrical arts, where the science is well-defined. Gene therapy, however, unlike mechanical and electrical engineering, is not a well-defined art, and hence, the use of a specific combination does not provide written description for a generic combination. Hence, Applicant's generic combination in no way is analogous to the proffered text of *In re Smythe*, because the art is not something well understood and defined.

Applicant further argues that verbatim correspondence between claim language and the specification is not required, but instead only is required to reasonably convey to the Artisan that

the inventor had possession of the subject matter in question, citing two decisions (Applicant's argument of 6/9/05, pp. 6-7, paragraph bridging).

Such is not persuasive. As has been argued above, Applicant's implicit disclosure does not reasonably convey that Applicant had possession of the generic combinations claimed (see above).

Hence, the rejection of the claims for comprising new matter is maintained.

Claim Rejections – 35 USC 102 – Nabel

Claims 17 and 19-36 remain rejected for reasons of record under 35 USC 102(b) as being anticipated by Nabel, et al. (U.S. Patent No. 5,863,904).

Response to Arguments

Applicant's arguments of 6/9/05 have been fully considered but are not found persuasive.

Applicant argues that, because they have demonstrated priority, such priority overcomes this rejection (Applicant's response of 6/9/05, p. 7, paragraph 3).

The argument is not persuasive because Applicants have not demonstrated priority (See above).

Therefore, the rejection of Claims 17 and 19-36 stands for reasons of record under 35 USC 102(b) as being anticipated by Nabel, et al. (U.S. Patent No. 5,863,904).

Claim Rejections – 35 USC 102 - Xiong

In light of Applicant's arguments, the rejection of Claims 17, 20-22, and 31 under 35 USC 102(b) as being anticipated by Xiong, et al. (Nature, 1993, 366: 701-704), are withdrawn.

Claim Rejections – 35 USC 103 – Xiong/Nabel

In light of Applicant's arguments, the rejections of Claims 17 and 19 under 35 USC 103(a) as being unpatentable over Xiong taken with Nabel et al. (Science 1990, 249: 1285-88), for reasons of record, are withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17, 20-24, 26-27, and 31 rejected under 35 U.S.C. 102(b) as being anticipated by Eastham, et al. (1995) Cancer Research: 55: 5151-55.

Applicant's claims encompass combinations comprising a catheter and a nucleic acid comprising a gene encoding p21. Such also may include a pharmaceutical carrier (such as for example, water or buffer), the nucleic acid may be expression vector, may comprise a viral promoter, which may be CMV, may be within a viral particle, and the nucleic acid may further comprise a second gene.

Eastham teaches recombinant adenoviruses comprising a transgene for p21, driven by the CMV promoter, with the SV40 polyA signal, which was grown in 293 cells (p. 5151, col. 2, paragraph 3). Moreover, such vectors were injected subcutaneously by a microliter syringe fitted with a 27 gauge need to inject a 50 microliter solution (i.e., pharmaceutical carrier) of

5000000000 PFU of virus into a tumor within an animal (p. 5152, paragraph 3). Hence, the combination of the claim is inherent, as the syringe is a catheter. For those embodiments comprising other genes on the same nucleic acid, the virus has other genes, otherwise the vector could not be packaged in 293 cells.

Therefore, Eastham anticipates the claims.

CONCLUSION

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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